

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

LOW MOLECULAR WEIGHT HEPARIN

Trevor W. Barrowcliffe
Head, Division of Haematology
National Institute for Biological Standards and Control
Potters Bar, Hertfordshire, UK

Edward A. Johnson
Formerly, Senior Scientist, Division of Chemistry
National Institute for Biological Standards and Control
Potters Bar, Hertfordshire, UK

Duncan P. Thomas
Consultant Medical Adviser
Bio Products Laboratory
Elstree, Hertfordshire
Formerly, Head, Division of Haematology
National Institute for Biological Standards and Control
Hertfordshire, UK

JOHN WILEY & SONS
CHICHESTER • NEW YORK • BRISBANE • TORONTO • SINGAPORE

Copyright © 1992 by John Wiley & Sons Ltd,
Baffins Lane, Chichester,
West Sussex PO19 1UD, England

All rights reserved.

No part of this book may be reproduced by any means,
or transmitted, or translated into a machine language
without the written permission of the publisher.

Other Wiley Editorial Offices

John Wiley & Sons, Inc., 605 Third Avenue,
New York, NY 10158-0012, USA

Jacaranda Wiley Ltd, G.P.O. Box 859, Brisbane,
Queensland 4001, Australia

John Wiley & Sons (Canada) Ltd, 22 Worcester Road,
 Rexdale, Ontario M9W 1L1, Canada

John Wiley & Sons (SEA) Pte Ltd, 37 Jalan Pemimpin #05-04,
Block B, Union Industrial Building, Singapore 2057

Library of Congress Cataloging-in-Publication Data

Barrowcliffe, Trevor W.

Low molecular weight heparin / Trevor W. Barrowcliffe, Edward A.
Johnson, Duncan P. Thomas.

p. cm.

Includes bibliographical references and index.

ISBN 0-471-93324-4

I. Heparin. I. Johnson, Edward A. II. Thomas, Duncan P., 1929-

III. Title.

RM666.H28B37 1992

615'.718—dc20

92-13987

CIP

British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library

ISBN 0 471 93324 4

Typeset in 10/12pt Palatino from author's disks by Text Processing Department,
John Wiley & Sons Ltd, Chichester
Printed and bound in Great Britain by Biddles Ltd, Guildford, Surrey

Introduction

Low molecular weight heparins are now licensed drugs in several European countries, and they are being increasingly used in the prophylaxis and treatment of venous thromboembolism, as well as in other disease states. The authors have been closely involved in the development of low molecular weight heparin over the past 15 years or so, particularly in relation to studying aspects of the biochemistry and standardisation of the drug, as well as in animal and human pharmacology studies. It has therefore seemed timely to bring together in a monograph the main aspects of this improved version of a drug that has long been a mainstay of anticoagulant and antithrombotic therapy, namely conventional, or unfractionated, heparin. While we have endeavoured to be reasonably comprehensive in our review of the field, we have not hesitated to emphasise the more important studies that have been carried out, and to give a personal viewpoint in areas where there has been disagreement. We have attempted to summarise the current position of low molecular weight heparin as an antithrombotic agent, acknowledging its undoubted advantages, but without endorsing some of the more extravagant claims that have been made.

This book brings together in one place the main elements of the history of low molecular weight heparin, from its early use in human volunteers, through extensive collaborative studies to establish an international standard for measuring activity, to the more recent large-scale clinical trials establishing safety and efficacy. The story is by no means complete, and much further work remains to be done. However, it is already clear that low molecular weight heparin represents a very significant addition to the list of effective drugs used for the prevention and treatment of thrombosis and related conditions.

TWB
EAJ
DPT

May 1992